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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,619	08/06/2001	Richard Apodaca	ORT-1474	8473

27777 7590 07/07/2003

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EXAMINER

WRIGHT, SONYA N

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 07/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/922,619	APODACA ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Sonya Wright	1626	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 1-6, 15, 20-22, 33, 36-38, 43-45, 48-51 and 56-69 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_ is/are allowed.

6) ☒ Claim(s) 1-6, 15, 20-22, 33, 36-38, 44, 45, 48-51, 56, 58 and 59 is/are rejected.

7) ☒ Claim(s) 43 and 57 is/are objected to.

8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____.  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

This action is in response to Applicant's amendment filed 6-12-03. Claims 1-6, 15, 20-22, 33, 36-38, 43-45, 48-51, and 56-59 are pending in this application.

The claim objections have been overcome with Applicant's amendments. The rejections under 35 U.S.C. 112 first and second paragraph in the action mailed 3-7-03 have been overcome with Applicant's amendments.

The finality of the previous office action is withdrawn in view of the following.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 15, 20-22, 33-38, 44, 45, 48, 49, 51, 56, 58, and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gotto et al., US Patent 5,580,883. This reference was cited as (CAPLUS AN 1996:754425, Goto et al.) in the Office Action mailed 5-16-02.

Determination of the scope and content of the prior art (MPEP §2141.01)

Goto et al. disclose aryloxypiperidines which are useful as antioxidants, cerebral nerve cell protectants, and in treating symptoms caused by cerebral ischemia, including dementia. See column 17, lines 51-64. Goto et al. generically teach the instant claims in column 2, lines 35-66, and column 3, lines 1-12. Goto et al. teach an example which is similar to the instant claims in Example 6, lines 11-20. Goto et al. generically teach the instant claims when, in the instant claims, X is O; n is 0, R5 is C1-C3 alkyl, one of R1, R2, and R3 is W wherein the remaining two are hydrogen, and W is morpholinyl.

The instant claims are drawn to aryloxypiperidines which are useful in treating diseases such as dementia, Alzheimer's disease, and epilepsy.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between Goto et al. and the instant claims is that in Example 6, Goto et al. teach a hydrogen on the piperidine ring which the instant claims disclose a C1-10 alkyl group on the nitrogen of the piperidine ring.

Further, Goto et al. teach homologs and positional isomers of the instant compounds in Example 6 as well as in the generic description in column 2, lines 35-66, and column 3, lines 1-12.

Finding of prima facie obviousness---rational and motivation (MPEP §2142-2143)

In Example 6 of Goto et al. there is a hydrogen on the piperidine nitrogen. In the instant claims there can be a –CH<sub>3</sub> group on the piperidine nitrogen. The difference between the instant compound and Example 6 of Goto et al. is –CH<sub>3</sub> versus hydrogen. However, it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results.

Nothing unobvious is seen in substituting the known claimed isomer for the structurally similar isomer, as taught by Goto et al., since such structurally related compounds suggest one another and would be expected to share common properties absent a showing of unexpected results. In re Norris, 84 USPQ 458 (1950). One of ordinary skill in the art would be motivated to use the teachings of Goto et al. to prepare the instant compounds in the expectation that positional isomers would be useful in treating diseases such as diseases such as dementia, Alzheimer's disease, and epilepsy. Further motivation is provided because Goto et al. teach examples which are similar to the instant compounds, and the instant methods of use (supra).

To those skilled in chemical art, one homolog is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used in treating diseases such as diseases such as dementia, Alzheimer's disease, and epilepsy. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988)):

- 1) Nature of invention.
- 2) State of prior art.
- 3) Level of ordinary skill in the art.

- 4) Level of predictability in the art
- 5) Amount of direction and guidance provided by the inventor.
- 6) Existence of working examples.
- 7) Breadth of claims.
- 8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

1) Nature of the invention.

Claim 49 is drawn to “a method of inhibiting histamine H3 receptor activity in a subject”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

2) State of the prior art.

The prior arts do not indicate that the instant compound is useful in “inhibiting histamine H3 receptor activity” in all cases.

3) Level of ordinary skill in the art.

There are a vast number of diseases related to histamine H3 receptor activity and Applicant does not give support for treating all forms of these disorders. The level of ordinary skill in the art is high.

4) Level of predictability in the art.

The various forms of diseases related to histamine H3 receptor activity have different causative agents, involve different cellular mechanisms, and, consequently,

differ in treatment protocol. The art pertaining to histamine H3 receptor activity remains highly unpredictable.

5) Amount of direction and guidance provided by the inventor.

Applicant provides limited guidance regarding biological activity on pages 137-139. Applicant provides background information on pages 1-4.

6) Existence of working examples.

Applicant provides 1 in vitro example and 1 in vivo example of how the instant compound is used.

7) Breadth of claims.

Claim 49 is extremely broad due to the large number of diseases related to histamine H3 receptor activity.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not use the claimed invention without undue experimentation.

It is suggested that Applicant incorporate the diseases related to histamine H3 receptor activity that are treated by the instant compound into claim 49.

***Claim Objections***

Claims 43 and 57 objected to as being dependent upon a rejected base claim.



***Response to Arguments***

Applicant's arguments, filed 6-12-03, regarding the claim objections and the rejections under 35 U.S.C. 112 have been fully considered. The claim objections and the rejections under 35 U.S.C. 112 first and second paragraph in the action mailed 3-7-03 have been overcome with Applicant's amendments.

However, upon further consideration, a 103 rejection is made in view of Goto et al., US Patent 5,580,883, and a 112 rejection is made, supra.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sonya Wright, whose telephone number is (703) 308-4539. The examiner can normally be reached on Monday-Friday from 8:00 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (703) 308-4537. The Unofficial fax phone number for this Group is (703) 308-7922. The Official fax phone numbers for this Group are (703) 308-4556 or 305-3592.

When filing a FAX in Technology Center 1600, please indicate in the Header (upper right) "Official" for papers that are to be entered into the file, and "Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [joseph.mckane@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees will not

communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-1235.



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Joseph K. McKane

Supervisory Patent Examiner

Group 1600

Sonya Wright

July 1, 2003